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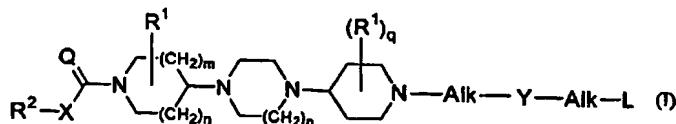
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(54) Title: SUBSTITUTED 1, 4-DI-PIPERIDIN-4-YL-PIPERAZINE DERIVATIVE COMBINED WITH AN OPIOID ANALGESIC AND THEIR USE FOR THE TREATMENT OF PAIN AND SIDE-EFFECTS ASSOCIATED WITH OPIOID-BASED TREATMENTS



and/or treatment of emesis, pain and/or nociception, in particular in opioidbased acute and chronic pain treatments, more in particular in inflammatory, postoperative, emergency room (ER), breakthrough, neuropathic and cancer pain treatments and the use of an NK<sub>1</sub>-receptor antagonist for the manufacture of a medicament for the prevention and/or treatment of respiratory depression in opioid-based treatments of pain. The pharmaceutical formulations according to the invention comprise a pharmaceutically acceptable carrier and, as active ingredients, a therapeutically effective amount of an opioid analgesic and NK<sub>1</sub> -antagonists according to the general Formula (I) the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, wherein all substituents are defined as in Claim 1. The pharmaceutical composition according to the invention reduces to a large extent a number of unwanted sideeffects associated with opioid analgesics, in particular emesis, respiratory depression and tolerance, thereby increasing the total tolerability of said opioids in pain treatment.

(57) **Abstract:** This invention concerns novel formulations for opioid-based treatments of pain and/or nociception comprising opioid analgesics and 1,4-di-piperidin-4-yl-piperazine derivatives having neurokinin antagonistic activity, in particular NK<sub>1</sub> antagonistic activity, the use of said formulation for the manufacture of a medicament for the prevention



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